PATENT CLAIMS

1. A modified human Factor VIII molecule being substantially non-immunogenic or less immunogenic than non-modified human Factor VIII and having essentially the same biological specificity and activity when used in vivo, comprising specifically altered amino acid residues compared with the non-modified parental molecule, wherein said altered amino acid residues cause a reduction or an elimination of one or more of T-cell epitopes which act in the parental non-modified molecule as MHC class II binding ligands and stimulate T-cells.

2. A modified Factor VIII molecule according to claim 1, wherein said alterations are made at one or more positions within one or more of the strings of contiguous amino acid residues present in the parental molecule as depicted in Table 1.

3. A modified Factor VIII molecule according to claim 2, wherein said alterations are made at one or more positions within one or more of the strings of contiguous amino acid residues present in the parental molecule as depicted in Table 2.

4. A modified Factor VIII molecule according to any of the claims 1 to 3, wherein said alterations are substitutions of 1 - 9 amino acid residues.

5. A modified Factor VIII molecule according to claim 4, wherein one, more or all of the amino acid residues at the following positions in a sequence string as depicted in Table 1 has been substituted :
197, 198, 199, 201, 202, 407, 411, 412, 419, 515, 517, 613, 617, 636, 637, 638, 639, 823, 1011, 1013, 1208, 1209, 1210, 1254, 1255, 1257, 1262, 1264, 1268, 1119, 1120, 1121, 1122, 1123.

6. A modified Factor VIII molecule according to claim 3, wherein in string P10 of Table 2 one, more or all of the following amino acid residue substitutions has been carried out:
I1208A, I1208T, I1208N;

I1209C;
M1210K, M1210N.

7. A modified Factor VIII molecule according to claim 3, wherein in peptide P8 of Table 2 one, more or all of the following amino acid residue substitutions has been carried out:
M1013K;
I1011A,I1011C,I1011D,I1011E,I1011G,I1011H,I1011K,
I1011P,I1011Q,I1011R,I1011S,I1011T.

8. A modified Factor VIII molecule according to claim 3, wherein in peptide P7 of Table 2 one, more or all of the following amino acid residue substitutions has been carried out:
V823A, V823D, V823E, V823G, V823H, V823N, V823P
V823S, V823T.

9. A modified Factor VIII molecule according to any of the claims 1 to 8, wherein when tested as a whole protein in a biological assay of induced cellular proliferation of human T-cells exhibits a stimulation index (SI) smaller than the parental molecule and smaller than 2 tested in parallel using cells from the same donor wherein said index is taken as the value of cellular proliferation scored following stimulation by the protein and divided by the value of cellular proliferation scored in control cells not in receipt of protein and wherein cellular proliferation is measured by any suitable means.

10. A DNA sequence coding for a Factor VIII molecule as defined in any of the claims 1 to 9.

11. A pharmaceutical composition comprising a modified Factor VIII molecule of any of the preceding claims, optionally together with a pharmaceutically acceptable carrier, diluent or excipient.

12. A peptide molecule selected from Table 1 having a potential MHC class II binding activity and created from the primary sequence of non-modified human

Factor VIII, whereby said peptide molecule has a stimulation index of > 1.8 in a biological assay of cellular proliferation, wherein said index is taken as the value of cellular proliferation scored following stimulation by a peptide and divided by the value of cellular proliferation scored in control cells not in receipt peptide and wherein cellular proliferation is measured by any suitable means.

13. A modified peptide molecule deriving from the peptide molecule of claim 12 by amino acid substitution, having a reduced or absent potential MHC class II binding activity expressed by a stimulation index of less than 2, whereby said index is taken as the value of cellular proliferation scored following stimulation by a peptide and divided by the value of cellular proliferation scored in control cells not in receipt peptide and wherein cellular proliferation is measured by any suitable means.

14. A DNA sequence coding for a peptide of claim 12 or 13.

15. Use of a peptide according to claim 13 for the manufacture of a modified Factor VIII molecule as defined in claim 1.

16. Use of a peptide according to claim 12 for the manufacture of a vaccine in order to reduce immunogenicity to Factor VIII in a patient.